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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,665	01/31/2002	Christine Leib-Mosch	10737-006001	2339

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Y. Rocky Tsao
Fish & Richardson
225 Franklin Street
Boston, MA 02110-2804

EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 05/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,665	LEIB-MOSCH ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-21* is/are pending in the application.

4a) Of the above claim(s) *13-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-12,20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment filed 3-1-04 has been entered. Claims 1-6, 8, 9, 11, 12, 20 and 21 have been amended. Claim 7 has been canceled. Claims 1-6 and 8-21 are pending, and claims 1-6, 8-12, 20 and 21 are under consideration.

Specification

1. The abstract of the disclosure is objected to because the amendment filed 3-1-04 indicates the abstract page is on page 30 of the specification, however, the abstract page is in fact on **page 31** of the specification. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 3 and 5 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention and is repeated for the reasons set forth in the preceding Official action mailed 8-27-03. Applicant's arguments filed 3-1-04 have been fully considered but they are not persuasive.

Applicants argue that "a [Y] region derived from a [X] nucleotide sequence" is synonymous to "a [Y] region in a [X] nucleotide sequence", i.e. a Y region from the X nucleotide sequence (amendment, bridging pages 7 and 8). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 8-27-03. The phrase "a [Y] region

derived from a [X] nucleotide sequence" means Y region can be a fragment of X nucleotide sequence or said fragment can be modified via various modification methods, such as adding a chemical group to said fragment, or removing or adding a few nucleotide sequences but maintaining the function of said fragment of X nucleotide. The specification fails to define the metes and bounds of what would be considered "derived from". Thus, claims 3 and 5 remain rejected under 35 U.S.C. 112 second paragraph.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-6, 8-12, 20 and 21 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention and is repeated for the reasons set forth in the preceding Official action mailed 8-27-03. Applicant's arguments filed 3-1-04 have been fully considered but they are not persuasive.

Applicants argue that in vitro data alone is sufficient to provide an asserted particular utility and the specification teaches how to use retroviral expression vector for expression of desired genes. Applicants further cite references Blaese et al., 1995, Grossman et al., 1994, Bordignon et al., 1995, and Gunzburg et al., 1996, and argue that these reference teach how to use expression vector for cell-specific expression of adenosine deaminase and LDL receptor for

sufficient expression at target site and provide therapeutic effect for adenosine deaminase and hypercholersterolaemia in vivo via various administration routes (amendment, p. 8-9). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 8-27-03. This rejection is an enablement rejection **not** a utility rejection. Applicants' argument that in vitro data is sufficient to provide an asserted utility is irrelevant to the present enablement rejection.

Although using retroviral vector for expression of a desired gene was known in the art and the cited references teach cell-specific expression of adenosine deaminase and LDL receptor in vivo, however, as discussed in the preceding Official action mailed 8-27-03, the art of gene therapy in vivo was unpredictable at the time of the invention. The main problem of gene therapy in vivo is the inability to deliver genes efficiently and to obtain sustained expression at target cells in vivo. The fate of the DNA vector itself, the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, and the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell all are important factors for a successful gene therapy in vivo. Each gene therapy has to be considered individually. One successful gene therapy can not be extrapolated into success for another gene therapy in vivo. The claims encompass using various promoter regions of different HERVs in a retroviral vector for cell-specific expression of desired genes, however, different promoter regions of HERVs have different expression ability at different cell types and the cited references do not use the promoter region of various HERVs for cell-specific expression in vivo. The

specification fails to provide adequate guidance and evidence for using a retroviral expression vector containing a HERV promoter sequence for cell-specific expression of a desired gene such that the expressed desired gene product would be sufficiently present at a target site to provide therapeutic effect for a particular disease or disorder *in vivo* via various administration routes. The specification also fails to provide adequate guidance for the correlation between the cell-specific expressed gene product and a particular disease or disorder. Thus, the specification fails to provide sufficient enabling disclosure for the full scope of the invention claimed. Therefore, the claims remain rejected under 35 U.S.C. 112 first paragraph.

Applicants argue that the references cited by examiner do not support that the state of gene therapy in vivo was not unpredictable at the time of the invention, and gene therapy has already been approved for treating head and neck squamous carcinoma and clinical trials for gene therapy started before the filing of the present application (amendment, p. 9-10). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 8-27-03 and the reasons set forth above.

Conclusion

No claim is allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for this group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.